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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,597	03/23/2001	Maurice J. Wolin	PP01658.002(035784/209107	7188

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EXAMINER	
HUFF, SHEELA JITENDRA	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/02/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/815,597	WOLIN ET AL.	
	Examiner	Art Unit	
	Sheela J Huff	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

The IDS filed 9/10/01, 1/08/02 and 1/07/02 have been considered. Initialed copies of the PTO-1449 are enclosed.

Priority

The provisional application 60/192047 is currently not available to the Examiner. Therefore, this action is based on the assumption that applicant only has priority to 3/23/01.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7, 13-15 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Freidberg et al Blood (11/16/00) Vol. 96(11) part 1 pp. 730a Abstract only. If applicant has priority to 60/192047, then this rejection will be withdrawn.

This reference discloses the Phase II treatment of non-Hodgkin's lymphoma with a combination of Rituximab (IDEC-C2B8) and IL-2. The patients were treated with low doses of subcutaneously administered IL-2 (1.2 mIU/m2) and 375 mg/m2 Rituximab. The dosage of 1.2 mIU/m2 for IL-2 reads on the ranges in the claims 13-15--the ranges in the claims are from about 2 mIU/m2 to about 12 mIU/m2, about 3 mIU/m2 to about 6 mIU/m2 and about 4.5 mIU/m2. The dose in the reference reads on the ranges in the claims because of the terminology "about".

Claims 1-7 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Yirinec et al. Blood vol. 94 p. 270b Abstract 4420.

This reference discloses the use of 375 mg/m2 Rituxan (IDEC-C2B8) and 4.5 mIU/m2 IL-2 to treat patients with low-grade or mantle cell non-Hodgkin's lymphomas. The IL-2 was administered subcutaneously.

Claims 1, 3 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated Hooijberg et al Cancer Research vol. 55 p. 2627 (1995).

This reference discloses the treatment of B cell cancers using a combination of anti CD20 antiboides and rhIL-2 (see abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freidberg et al Blood (11/16/00) Vol. 96(11) part 1 pp. 730a Abstract only, in view of

applicant's admission on page 18, line 11 to page 21. If applicant has priority to 60/192047, then this rejection will be withdrawn.

The reference has been discussed above.

The only difference between the instant application and the reference is the treatment regiment and the composition of the IL-2 (claims 8-10).

On pages 18-21, applicant admits that functional variants of IL-2 are well known in the art (see specifically page 18, line 30 to page 19, line12). On page 19 bottom to page 21, applicant admits that the stabilized forms of IL-2 are art known.

Optimization of treatment conditions and dosages is within the purview of one skilled in the art. In view of the above, it would have been obvious to one of ordinary skill in the art to optimize the treatment and dosages with the expected benefits of treating non-Hodgkin's lymphoma. It also would have been obvious to use any known IL-2 variant or stabilized form of IL-2 in view of applicant's admission that they are known in the art. The use of art known equivalents for the same purpose is obvious.

Claims 1-19 are rejected under 35 U.S.C. 103 as being obvious over Yirinec et al. Blood vol. 94 p. 270b Abstract 4420, in view of applicant's admission on page 18, line 11 to page 21.

The reference has been discussed above.

The only difference between the instant application and the reference is the treatment regiment and the composition of the IL-2 (claims 8-10).

On pages 18-21, applicant admits that functional variants of IL-2 are well known in the art (see specifically page 18, line 30 to page 19, line12). On page 19 bottom to page 21, applicant admits that the stabilized forms of IL-2 are art known.

Optimization of treatment conditions and dosages is within the purview of one skilled in the art.

In view of the above, it would have been obvious to one of ordinary skill in the art to optimize the treatment and dosages with the expected benefits of treating non-Hodgkin's lymphoma. It also would have been obvious to use any known IL-2 variant or stabilized form of IL-2 in view of applicant's admission that they are known in the art. The use of art known equivalents for the same purpose is obvious.

Claims 1, 3-5 and 7-19 are rejected under 35 U.S.C. 103 as being obvious over Hooijberg et al Cancer Research vol. 55 p. 2627 (1995), in view of applicant's admission on page 4, line 13 and page 18, line 11 to page 21.

The reference has been discussed above.

The only difference between the instant application and the reference is the treatment regiment and the composition of the IL-2 (claims 8-10) and IDEC-C2B8 and the subcutaneous administration.

On page 4, applicant admits that IDEC-C2B8 is well known in the art.

On pages 18-21, applicant admits that functional variants of IL-2 are well known in the art (see specifically page 18, line 30 to page 19, line12). On page 19 bottom to page 21, applicant admits that the stabilized forms of IL-2 are art known.

Optimization of treatment conditions and dosages is within the purview of one skilled in the art.

In view of the above, it would have been obvious to one of ordinary skill in the art to optimize the treatment and dosages with the expected benefits of treating B-cell lymphoma. It also would have been obvious to use any known IL-2 variant or stabilized form of IL-2 in view of applicant's admission that they are known in the art. The use of art known equivalents for the same purpose is obvious. For the same reason the use of IDEC-C2B8 (a known anti-CD20 antibody) would readily be obvious to one skilled in the art. The route of administration is within the purview of one skilled in the art unless criticality for the subcutaneous route can be shown.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/09160 or US 6455043 (priority to 8/11/98) in view of), in view of applicant's admission on page 18, line 11 to page 21.

The WO document is the WO of the patent 6455043.

Both references disclose a combined therapeutic regime for Non-Hodgkin's B cell lymphomas suing anti-CD20 antibodies (specifically IDEC-C2B8) and cytokines (IL-2) (see abstract of both, col. 3, lines 11-35, col. 2, line 54-56, col. 13+ of patent and pages 5-6 and 25+ of the WO). The dose of IDEC-C2B8 used ranges from 125-375 mg/m2 (col. 8, line 60-64 of patent and page 16 of WO).

The only difference between the instant application and the references is a specific showing of the combination therapy.

However, in view of the explicit suggestion in the reference to use IL-2 and IDEC-C2B8 to treat non-Hodgkin's B cell lymphomas, one of ordinary skill in the art would immediately envisage the treatment.

On pages 18-21, applicant admits that functional variants of IL-2 are well known in the art (see specifically page 18, line 30 to page 19, line12). On page 19 bottom to page 21, applicant admits that the stabilized forms of IL-2 are art known.

Optimization of treatment conditions and dosages is within the purview of one skilled in the art.

Thus, in view of the suggestion in the references to use IL-2 and IDEC-C2B8 to treat non-Hodgkin's B cell lymphomas, it would have been obvious to one of ordinary skill in the art at the time of the invention to use IL-2 and IDEC-C2B8 to treat non-Hodgkin's B cell lymphomas. It also would have been obvious to one of ordinary skill in the art to optimize the treatment and dosages with the expected benefits of treating B-cell lymphoma. It also would have been obvious to use any known IL-2 variant or stabilized form of IL-2 in view of applicant's admission that they are known in the art. The use of art known equivalents for the same purpose is obvious. The route of administration is within the purview of one skilled in the art unless criticality for the subcutaneous route can be shown.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 703-305-

7866. The examiner can normally be reached on Tuesday 5:30am-11:30am and Fridays 6:00am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh